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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,780	12/03/2001	Norman R. Wainwright	1413.001000B/RWE/MTT	7532

26111 7590 06/03/2004

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EXAMINER	
GUPTA, ANISH	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,780	WAINWRIGHT ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71,72 and 80-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71,72 and 80-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed, 12-03-01, is acknowledged. Claims 71 and 80 were amended. Claims 82-83 were added. Claims 71-72 and 80-83 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 80-83 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 80-83 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step that changes the capacitance, resistance, or acoustic wave of the solid phase. The claim as stated, states that the method starts with the contacting of the protein to the support and ends with the detection of changes in capacitance, resistance, or acoustic wave. The claim is, however, silent as to the process steps involved in achieving these changes.

In claim 80, it is unclear how the "standard solutions" and the changes therein are involved in the method. That is, it is unclear what are "the changes" in standard solutions of endotoxin binding protein?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 71-72 and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al.

The claims are drawn to a biosensor device comprising an endotoxin binding protein from horseshoe crab *Limulus polyphemus*, immobilized on a solid phase support, which is either quartz or silicon.

The reference discloses the contacting of ambeocyte lyaste from the hemolymph of the horseshoe crab limulus polyphemus to a synthetic plastic polymer support to measure endotoxin in a fluid sample (see abstract). The reference discloses the use of synthetic polymers including silicon elastomer, thereby meeting the limitation of claim 72 (see col. 4, lines 40-45). Although the refernence discloses that the ameocyte lysate is bound to the endotoxin, which are bound to the silicon elastomer, the reference still read on the claims since they components to the device of the reference and the claims are the same, i.e. solid support and endotoxin binding protein.

It is noted that the primary reference does not specifically teach that the protein from the horseshoe crab corresponds to SEQ. ID. No. 1. However, since the protein is from the same source, horseshoe crab, and has the same activity, endotoxin binding, the sequence would necessarily have to be the same.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 71-72 and 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levin (US 3915805) et al. in view of Rice (US 4236893).

The claims are drawn to a biosensor device comprising an endotoxin binding protein from horseshoe crab *Limulus polyphemus*, immobilized on a solid phase support, which is either quartz or silicon and a method of determining endotoxins in a sample.

The reference of Levin et al. teach a method of determining endotoxin in a sample using a protein in the amebocytes of the horseshoe crab (Limuls) (see abstract). The reference states that the protein is a sensitive indicator of bacterial endotoxin (see col. 1, lines 58-60). Further, the horseshoe crab protein can detect as little as five tenthousandths microgram of endotoxin per milliliter (see col. 2, lines 15-18). The difference between the prior art and the instant application is that the reference does no teach the use of a biosensor as claimed in claim 80.

However, Rice teaches a method of deterring antibodies a sample that uses a piezoelectric oscillator having bound to the surface thereof an antigen specific for the antibody being determined (see abstract). The reference states that the method utilizes the measurement of frequency change to antigen/antibody binding on the quartz surface to determine the amount of antibody present in a sample (see col. 4, lines 7-20). The reference states that the solid support is a quartz crystal (see col. 3, lines 24). The reference states that not only antibodies but other binding reagents such as bacterium Straphlococcus aureus or other cells which have surface receptors for certain types of immunoglobulins can be used (see col. 2, lines 46-59). The reference states that this means of analysis is inexpensive and unsophisticated and the results obtained are "rapid, accurate and objective measurements." (see col. 2, lines 59-68). It should be noted that the association between protein from the horseshoe crab and endotoxin is similar to the antibody/antigen binding. Given this similarity, it would have been obvious to one of ordinary skill in the art to substitute the endotoxin binding protein from the horse crab for the antigen on the quartz to measure the amount of endotoxin in a solution. Note that the horseshoe crab protein can detect as little as five ten thousandths microgram of endotoxin per milliliter and thus is an effective means of measuring endotoxin. One would be motivated to make such a substitution because not only is the horseshoe protein an effective means of measuring endotoxin, but the system of measurement is rapid, accurate and objective.

It is noted that the primary reference does not specifically teach that the protein from the horseshoe crab corresponds to SEQ. ID. No. 1. However, since the protein is from the same source, horseshoe crab, and has the same activity, endotoxin binding, the sequence would necessarily have to be the same.

5. Claims 71-72 and 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levin (US 3915805) et al. in view of Olivera et al. (US4242096).

The claims are drawn to a biosensor device comprising an endotoxin binding protein from horseshoe crab *Limulus polyphemus*, immobilized on a solid phase support, which is either quartz or silicon and a method of determining endotoxins in a sample.

The reference of Levin et al. teach a method of determining endotoxin in a sample using a protein in the amebocytes of the horseshoe crab (Limuls) (see abstract). The reference states that the protein is a sensitive indicator of bacterial endotoxin (see col. 1, lines 58-60). Further, the horseshoe crab protein can detect as little as five ten thousandths microgram of endotoxin per milliliter (see col. 2, lines 15-18). The difference between the prior art and the instant application is that the reference does no teach the use of a biosensor as claimed in claim 80.

However, Rice teaches a method of deterring antigens in a sample that uses a piezoelectric oscillator to determine a specific antigen in an unknown liquid sample (see col. 2, lines 63-65). The reference states that the method involves contacting the liquid sample with a predetermined amount of an antibody specific for the antigen being determined in a composite comprising piezoelectric oscillator having immobilized thereon, in biologically active configuration, an antigen or mixture of proteins containing the antigen to be determined and the composite having a predetermined frequency (see paragraph bridging col. 2 and 3). The change in frequency of the oscillator can be used to determine the amount of antigen in a sample. It is stated that the method is simple and uses inexpensive instrumentation (see col. 3, lines 12-15). Further, the method does not involve labeling techniques or the problems therewith (see col. 3, lines 26-35). The reference states that the method can be used for analysis of a variety of antigenic materials ranging from low molecular weigh to compounds to large macromolecules (see col. 3, lines 36-40). It should be noted that the

association between protein from the horseshoe crab and endotoxin is similar to the antibody/antigen binding. Given this similarity, it would have been obvious to one of ordinary skill in the art to substitute the endotoxin binding protein from the horse crab for the antigen on the quartz to measure the amount of endotoxin in a solution. Note that the horseshoe crab protein can detect as little as five-tenthousandths microgram of endotoxin per milliliter and thus is an effective means of measuring endotoxin. One would be motivated to make such a substitution because not only is the horseshoe protein an effective means of measuring endotoxin, but the system of measurement is rapid, inexpensive and does not use labeling techniques.

It is noted that the primary reference does not specifically teach that the protein from the horseshoe crab corresponds to SEQ. ID. No. 1. However, since the protein is from the same source, horseshoe crab, and has the same activity, endotoxin binding, the sequence would necessarily have to be the same.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 71-72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. US 6,222,021. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims are drawn to a biosensor device comprising an endotoxin binding protein from horseshoe crab *Limulus polyphemus*, immobilized on a solid phase support, which is either quartz or silicon.

The US Patent claims a fragment of endotoxin binding protein that is immobilized on a solid phase support (see claim 1 and 3). The US Patent states that the immobilized binding protein is a biosensor device (see claim 5). The solid support is a silicone or quartz support, similar to the claimed support in claim 72 (see claim 6). Therefore, the reference sufficiently disclose the invention to render the instant application claimed invention as not patentably distinct.

7. Claims 80-83 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. US 6,222,021 in view of Oliveira et al. and Levin et al.. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims are drawn to a biosensor device comprising an endotoxin binding protein from horseshoe crab *Limulus polyphemus*, immobilized on a solid phase support, which is either quartz or silicon.

The US Patent claims a fragment of endotoxin binding protein that is immobilized on a solid phase support (see claim 1 and 3). The US Patent states that the immobilized binding protein is a biosensor device (see claim 5). The solid support is a silicone or quartz support, similar to the

claimed support in claim 72 (see claim 6). The difference between the US Patent and the instant application is that US Patent does not teach the method of assaying to measure endotoxin in a sample.

However, Olivera generally teaches that biosensors can be used to measure amount of antigen in a sample (see abstract). The reference of Levin teach that The reference of Levin et al. teach a method of determining endotoxin in a sample using a protein in the amebocytes of the horseshoe crab (Limuls) (see abstract). The reference states that the protein is a sensitive indicator of bacterial endotoxin (see col. 1, lines 58-60). Further, the horseshoe crab protein can detect as little as five ten thousandths microgram of endotoxin per milliliter (see col. 2, lines 15-18). Therefore, it would have been obvious to one of ordinary skill in the art to use the biosensor disclosed in the US Patent for an assay method to measure endotoxin because the protein is a strong indicator of bacterial endotoxin.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback , can normally be reached on (571) 272-0961. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

5/31/04

Anish Gupta

Patent Examiner